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Case Report

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Get two with one: bevacizumab treatment in hereditary hemorrhagic telangiectasia with concomitant cirrhosis

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ABSTRACT

Hereditary hemorrhagic telangiectasia (HHT) or Osler-Weber-Rendu syndrome is a birth defect of the blood vessels that causes telangiectasias and arteriovenous malformations. HHT is a rare, autosomal dominant vascular disorder affecting approximately 1 in 8000 people. This multisystem angiogenic disorder is genetically and phenotypically variable, with the most common symptom being severe and recurrent epistaxis. ALK1, TGF-β, and VEGF are involved in its pathogenesis. VEGF increases mitotic activity in vascular endothelial cells, leading to uncontrolled angiogenesis and the formation of fragile vessels. Bevacizumab is used in the treatment of HHT by inhibiting VEGF. We present our patient, who developed hepatic encephalopathy due to hemorrhages with diffuse telangiectasias of the skin and tongue due to HHT and achieved an effective response to both conditions with bevacizumab.

Keywords: Bevacizumab, hereditary hemorrhagic telangiectasia, Osler-Weber-Rendu syndrome, telangiectasia

INTRODUCTION

Osler-Weber-Rendu syndrome, also known as hereditary hemorrhagic telangiectasia (HHT), is a developmental disorder of the vascular system that causes telangiectasias and arteriovenous malformations.[1] Although it is one of the most common monogenic disorders, it is usually undiagnosed. The most common features are epistaxis and telangiectasias on the lips, hands, and oral mucosa, which usually have a mild course. The management of vascular malformations in HHT is very important. Telangiectasias in the nasal and gastrointestinal mucosa and arteriovenous malformations in the brain may often present with bleeding.[2] Bevacizumab is a vascular endothelial growth factor (VEGF) inhibitor and reduces epistaxis, telangiectasia, and iron deficiency anemia.

We present our patient, who developed hepatic encephalopathy due to hemorrhage with diffuse telangiectasias on the skin and tongue due to HHT and achieved an effective response to both conditions with bevacizumab.

CASE

A 65-year-old woman was diagnosed with chronic liver parenchymal disease (CLD) and HHT. She was admitted to the hematology outpatient clinic due to the development of telangiectasias in the mouth, especially on the tongue, and in different parts of her body. Her cognitive functions declined, and laboratory tests revealed hemoglobulin (Hb) 9 g/dl and increased liver function tests. The patient was consulted for gastroenterology, and her ammonia level was 97 µmol/L. She was evaluated for decompensated cirrhosis and hepatic encephalopathy stage 1. With off-label admission, bevacizumab was started at a dose of 5 mg/kg at 2-week intervals. One week after the first dose, ammonia decreased to 51 µmol/L, and cognitive functions returned to normal. It decreased to 25 µmol/L at the end of the second week and always remained in the normal range (**Figure 1**). Hb levels increased to 12.1 g/dl in the fourth week without any other treatment (**Figure 2**). The patient's tongue telangiectasias completely normalized at the beginning of the second week.

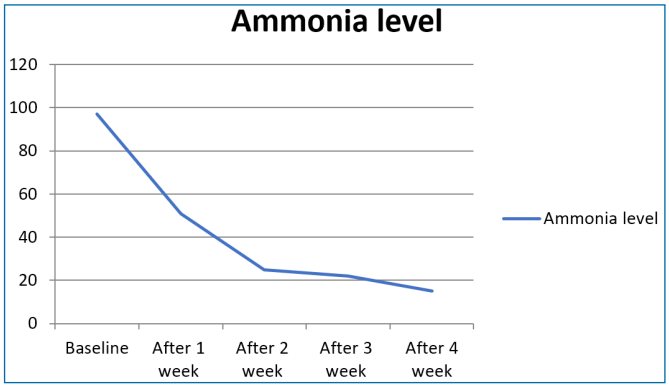

Figure 1. Ammonia levels (µmol/L) after bevacizumab treatment

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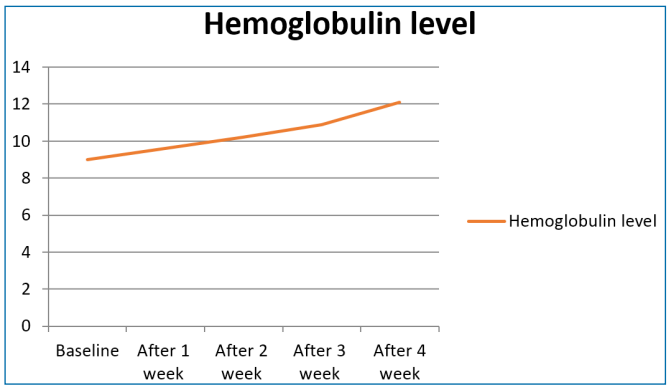

Figure 2. Hemoglobulin levels (g/dl) after bevacizumab treatment

DISCUSSION

HHT is a genetic disorder characterized by uncontrolled multisystem angiogenesis with epistaxis, telangiectasias, gastrointestinal bleeding, iron deficiency anemia, and arteriovenous malformations. It is usually associated with increased VEGF.[1] HHT is a rare, autosomal dominant vascular disease that occurs in approximately 1 in 8000 individuals.[1,2] This multisystem angiogenic disorder is genetically and phenotypically variable, and the most common symptom is severe and recurrent epistaxis. Other clinical features include mucocutaneous telangiectasias, gastrointestinal bleeding, iron deficiency anemia, and arteriovenous malformations, most commonly in the lung, brain, and liver.[3] ALK1, TGF-β, and VEGF play a role in its pathogenesis.[4]

VEGF increases mitotic activity in vascular endothelial cells and leads to uncontrolled angiogenesis and the formation of fragile vessels.[5] Bevacizumab is used in the treatment of HHT by inhibiting VEGF.

Hemorrhages in the CLD may lead to decompensation and the development of hepatic encephalopathy, as in our patient. After bevacizumab, ammonia levels normalized in our patient in two weeks.

Epperla et al.[6] gave bevacizumab to people who had bleeding and telangiectasias and saw that their Hb levels rose from 10 g/dl to 14.2 g/dl in 4 weeks without any other treatment to help. In our patient, an increase of 3 g/dl was observed during the same period. The treatment dose was 10 mg/kg/2 weeks in the case of Epperla et al. and 5 mg/kg/2 weeks in our case. Again, in this case, significant improvement was observed in telangiectasias during the same period as in ours.

CONCLUSION

In HHT, bevacizumab inhibited VEGF, preventing the development of fragile vessels and telangiectasias and preventing the development of decompensated cirrhosis and hepatic encephalopathy due to hemorrhage.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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